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RESPONSE UNDER 37 C.F.R. § 1.116
EXPEDITED PROCEDURE – Art Unit 2652
Attorney Docket No. 59200-8015.US00



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:

KONDEJEWSKI, *et al.*

APPLICATION No.: 09/603,832

FILED: June 26, 2000

FOR: **POLYPEPTIDE COMPOSITIONS FORMED
USING A COILED-COIL TEMPLATE AND
METHODS OF USE**

EXAMINER: CHAKRABARTI, ARUN K.

ART UNIT: 1655

CONFIRMATION No: 2421

RECEIVED

JUL 31 2002

TECH CENTER 1000/2000

Amendment Under 37 C.F.R. § 1.116 - Transmittal

Box AF
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

1. Transmitted herewith are the following:

- ☒ A Response/Amendment Under 37 CFR 1.116 (After Final)
- ☒ A Petition for Three-Month Extension of Time
- ☒ A Notice of Appeal
- ☐ A Terminal Disclaimer
- ☐ Sequence Listing printout, floppy diskette, matching declaration
- ☐ Information Disclosure Statement, Form 1449, References
- ☐ Check in the amount of \$

2. Entity Status

- ☒ Small Entity Status (37 CFR 1.9 and 1.27) has been established by a previously submitted Small Entity Statement.

3. Conditional Petition for Extension of Time

An Extension of Time is requested to provide for timely filing if necessary for timely filing of this transmittal and enclosures.

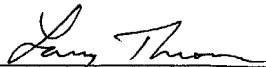
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4. Provisional Fee Authorization

Please charge any underpayment in fees for timely filing of this transmittal and enclosures to Deposit Account No. 50-2207.

Respectfully submitted,
Perkins Coie LLP

Date: 7-25-02



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EXAMINER: Chakrabarti, A.

ART UNIT: 1655

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TECH CENTER 1609/25

Response to Final Office Action Under 37 C.F.R. §1.116

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This amendment is in response to the Office Action mailed January 25, 2002 in the above-identified application. Reconsideration of the rejections set forth in the Office Action is respectfully requested. Applicant petitions the Commissioner for a 3-month extension of time. A separate petition accompanies this amendment. Claims 1-9 are currently under examination.

I. Rejections Under 35 U.S.C. §103

Claims 1-5 were rejected under 35 U.S.C. §103(a) as being obvious over Anderson (U.S. Patent No. 6,242,213 B1) in view of Yan (U.S. Patent 5,856,928). Claims 1-9 were rejected under 35 U.S.C. §103(a) as being obvious over Anderson (U.S. Patent No. 6,242,213 B1) in view of Yan (U.S. Patent 5,856,928), further in view of Prusiner *et al.* (U.S. Patent 5,793,901). These rejections are respectfully traversed for the following reasons.

A. The Present Invention

The present invention, as embodied in amended claim 1, is directed to a coiled-coil polypeptide composition comprising a template of the form $(ab_cde_fg)_n$, where the sequence formed by the positions $(b_cde_fg)_n$ is a sequence of amino acids from a solvent-accessible region of an epitope from a selected protein, where the region is not in a coiled-coil conformation in its native state.

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Although there has been considerable interest in preparing compositions capable of mimicking or blocking conformationally distinct protein-protein interactions in cells, and for generating antibodies capable of recognizing distinct protein conformations, the tools necessary to achieve this preparation have not been available. The present invention addresses this problem, and solves it by inserting solvent-accessible residues of an epitope from a region of a protein that is normally not in a coiled-coil conformation into a conformationally-restricted, stabilized coiled-coil template.

B. The Cited Art

Anderson discloses isolated DNA molecules encoding RANK-L, and briefly describes leucine zipper domains and proteins that form coiled-coil dimers in their native state (column 6, lines 63-65). The reference is not concerned with the problem addressed by the present invention, nor does it suggest Applicants' solution. In particular, the reference does not show or suggest inserting solvent-accessible residues of an epitope from a region of a protein that is normally not in a coiled-coil conformation into a conformationally-restricted, stabilized coiled-coil template.

Yan discloses a method for representing and evaluating protein and gene sequences. A combinatorial method assigns nucleotide bases or amino acids unique numbers, making use of "the information generating properties of prime and odd numbers." A number of examples are used to illustrate that numerical patterns manifest structural patterns. One of these examples is the prion protein. Using the "prime heptad scan" method, Yan concludes that heptads in prion protein chains are "highly regular," that prion proteins are of ancient origin, and that prion proteins have fibrous chains. However, Yan is not concerned with the problem addressed by the present invention, nor does it suggest Applicants' solution for the same reasons as were applied to Anderson.

Prusiner et al. describe a transgenic animal containing an artificial prion protein. Prusiner et al. is not concerned with the problem addressed by the present invention, nor does the reference suggest Applicants' solution for the same reasons as were applied to Anderson.

C. Analysis

C1. Legal Standard for Nonobviousness.

In determining whether an invention is nonobvious, the PTO has the burden of establishing a case of *prima facie* obviousness. A proper analysis under 35 U.S.C. §103 requires consideration of whether the prior art would have suggested to those of ordinary skill in the art

that they should make the claimed composition or device, or carry out the claimed process and whether the prior art would have also revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. See MPEP §2142, citing *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991).

"As applied to the determination of patentability *vel non* when the issue is obviousness, 'it is fundamental that rejections under 35 U.S.C. §103 must be based on evidence comprehended by the language of that section.'" (quoting *In re Grasselli*, 713 F.2d 731, 739, 218 USPQ 769, 775 (Fed. Cir. 1983)); *In re Sang Su Lee*, 277 F.3d 1338, 61 USPQ2d 1430 (Fed. Cir. 2002). The essential factual evidence on the issue of obviousness is set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966) and extensive ensuing precedent. When patentability turns on the question of obviousness, the search for and analysis of the prior art includes evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the references relied on as evidence of obviousness. See, e.g., *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1351-52, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001) ("the central question is whether there is reason to combine [the] references," a question of fact drawing on the *Graham* factors).

"The factual inquiry whether to combine references must be thorough and searching." *Id.* It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with. See, e.g., *Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1124-25, 56 USPQ2d 1456, 1459 (Fed. Cir. 2000) ("a showing of a suggestion, teaching, or motivation to combine the prior art references is an 'essential component of an obviousness holding'" (quoting *C.R. Bard, Inc. v. M3 Systems, Inc.*, 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed. Cir. 1998)); *In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references."); *In re Dance*, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998) (there must be some motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant); *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988) ("teachings of references can be combined only if there is some suggestion or incentive to do so.") (emphasis in original) (quoting *ACS Hosp. Sys., Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984)).

See, also, *In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000)

("particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed"); and *In re Fritch*, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (the examiner can satisfy the burden of showing obviousness of the combination "only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references").

Thus, for a combination of references to render a claimed invention obvious under 35 U.S.C §103, that combination must provide not only a suggestion of the present invention, but also a reasonable expectation of success in reaching that invention. Furthermore, the Examiner must articulate reasons for his or her decision. Under these standards, and as discussed below, the Examiner has not made a *prima facie* case of obviousness.

C2. Lack of suggestion in the prior art; Examiner's statements are conclusory

In order for the prior art to provide motivation for combining references along the lines of the invention, the prior art must recognize the advantages to be gained by such combination. As noted above, none of the references cited is concerned with the problem of preparing compositions capable of mimicing or blocking conformationally distinct protein-protein interactions in cells, or for generating antibodies capable of recognizing distinct protein conformations. Nor do any of the references suggest the possibility of addressing the problem successfully by inserting solvent-accessible residues of an epitope from a region of a protein that is normally not in a coiled-coil conformation into a conformationally-restricted, stabilized coiled-coil template.

The Examiner states that Anderson could be combined with Yan to "achieve the express advantages, as noted by Yan, of an invention that can detect gelling proteins – fibrinogen, beta amyloid, and prions – which are either wound-healing or disease-causing agents." (Paper No. 10, page 4). However, this statement does not adequately address the issue of motivation to combine. There is no support for the selection and combination of the Yan and Anderson references to render obvious that which Applicants have described. A method of determining which proteins are gelling or fibrous is of no use in the instant invention, and provides no motivation to combine the two references to achieve Applicant's composition.

As noted above, Yan uses numerical patterns based on sequence information to represent structural patterns. Following the identification of "prime heptads" in prion proteins, the ratio of prime to nonprime heptads, the relative proportion of these prime heptads in different areas of the proteins, and the number of exons, Yan concludes that prion proteins are of ancient origin and have fibrous chains like fibrinogen, collagen, etc. Yan's observation that prion proteins are

disease-causing agents is not a result of Yan's numerical analysis, nor is it even novel. Prion proteins have been known to be disease-causing agents for many years (see, e.g. page 10, lines 10-13 of the instant specification). These conclusions and observations fail to provide any suggestion or motivation for inserting the solvent-accessible amino acid residues of the prion protein into a conformationally-restricted, stabilized coiled-coil template. Rather, they provide support for the use of Yan's method to identify various patterns in proteins and nucleic acids.

The factual question of motivation can not be resolved on subjective belief and unknown authority. *In re Sang Su Lee*, 277 F.3d 1338, 61 USPQ2d 1430 (Fed. Cir. 2002). It is improper, in determining whether a person of ordinary skill would have been led to this combination of references, simply to "[use] that which the inventor taught against its teacher." *W.L. Gore v. Garlock, Inc.*, 721 F.2d 1540, 1553, 220 USPQ 303 (Fed. Cir. 1983). The PTO must articulate reasons for its decision. Broad, conclusory statements about the teachings of multiple references, standing alone, are not evidence. *Brown & Williamson Tobacco Corp. v Philip Morris, Inc.* 229 F.3d 1120; 56 USPQ2d 1456 (Fed. Cir. 2000). The Examiner's conclusory statement that Yan's method of identifying gelling proteins provides motivation for the instant invention does not constitute reasoned decisionmaking. The reasoning as to what would motivate a person of ordinary skill in the art to combine the two references is not clear.

The Examiner points to column 6, lines 17-18 of Prusiner *et al.* as providing the motivation necessary to achieve the present invention. However, the paragraph beginning on column 6, lines 17-18 is concerned with testing samples for the presence of prions by creating two groups of non-human mammals which have their genome altered so that they are susceptible to infection with prions which generally only infect a genetically diverse animal. The reference provides no suggestion or motivation for inserting the solvent-accessible amino acid residues of the prion protein into a conformationally-restricted, stabilized coiled-coil template.

In the absence of such a suggestion, and failing to recognize the problem addressed by the present invention, and its solution, the prior art cannot be said to provide a suggestion or motivation for the claimed invention. Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §103(a).

V. Conclusion

In view of the above remarks, the applicants submit that the claims pending are in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4405.

Respectfully submitted,



Date: 7-25-02

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